## REMARKS

Applicants respectfully request reconsideration and allowance of this application in view of the amendments above and the following comments.

The Examiner rejected claim 8 under 35 USC §112, second paragraph, as failing to comply with the enablement requirement, stating that claim 8 contains subject matter which was not described in the specification in such a way to enable one skilled in the art to make or use the invention. In response, applicants have amended claim 8 to recite a method of treating a bacterial infection. Applicants point out that support for amended claim 8 appears on page 1, paragraph 1 of applicants' specification. Applicants also pointed out that the product claims provided protection against unauthorized use thereof to treat parasites and viruses anyway.

The Examiner rejected claims 3, 4, 6 and 7 under 35 USC §112, second paragraph, as being indefinite. In response, Applicants have amended the claims in a manner which Applicants believe over comes each of the Examiner's concerns. In claims 3 and 4, Applicants have amended these claims to replace the words "one of" with the words "at least one member selected from the group consisting of". Regarding claims 6 and 7, Applicants have amended the claims by rewriting them to recite "water soluble antiphlogistic antibiotics salts" and Applicants have deleted the recitation of "tablet and/or molded body form". Applicants have introduced new dependent claims 11 and 12 that incorporate the recitation of "tablet" and/or "molded body form" respectively.

Applicants do not believe that any of the amendments introduce new matter. An early notice to that effect is earnestly solicited.

The Examiner rejected claims 1-10 under 35 U.S.C. 102(b) as being anticipated by or in the alternative under 35 U.S.C. 103(a) as being obvious over Bayens et al. (J. of Controlled Release, 1998, Vol. 52, pages 215-2220), Renard et al. (J. Fr. Ophtalmol., 1996, Vol. 19, No. 11, pages 689-695) or Golub et al., (U.S. Patent No. 5,459,135).

In response, Applicants point out that each and every element recited in a claim must be found in a single prior art reference and arranged as in the claims. Applicants claim a salt comprising a cationic component and an anionic component. The Bayens reference does not teach a salt comprising a cationic component and an anionic component, but in fact describes eye drops and an ocular insert containing a combination of gentamicin sulphate and dexamethasone phosphate. Nowhere in the Bayens reference does Bayens teach the formation of a *salt with a low solubility in water* (formation of precipitate) from gentamicin sulphate and dexamethasone phosphate. Neither does Bayens teach a salt whose cationic component is formed from gentamicin and whose anionic component comprises dexamethasone phosphate.

Applicants claim salts whose cationic component contains at least one representative of the antibiotics gentamicin, clindamycin, neomycin, streptomycin, tetracycline, doxicycline, oxytetracycline and whose anionic component contains at least one representative of the antiphlogistics ibuprofen, naproxen, indomethacin, dexamethasone-21-phosphate, dexamethasone-21-sulphate, triamcinolone-21-phosphate and triamcinolone-21-sulphate. In this way, the structure of Applicants' salt is unambiguously described. This means that the cationic

component of the salt contains the protonated antibiotics base and the anionic component contains at least one anion of the antiphlogistics. In Applicants' description, it is clearly indicated that these *salts have low solubility in water.*

The formation of a low solubility salt may appear, at first blush, to be possible in the case of the recipes described in Bayens, however, in the comparative eye drop solution; page 216, 2.1 Materials, paragraph 2) very low gentamicin sulphate and dexamethasone phosphate concentrations are used (0.3% and 0.1% respectively). For this reason, no formation of precipitate was observed. For the formation of precipitates, higher gentamicin sulphate and dexamethasone phosphate concentrations are required (compare practical example no. 1 of the present application (150 mg/ml and 120 mg/ 2ml respectively)). Bayens, et al., were consequently not aware of the formation of low solubility gentamicin dexamethasone salts, otherwise reference would not have been made in Bayens, et al., (page 216, 2.2 Insert composition and manufacture, paragraph 1) to the prolongation of the gentamicin sulphate release by the formation of a solid dispersion of gentamicin sulphate in CAP (cellulose acetate phthalate). Additionally, Bayens, et al., describes in "2.2 Insert composition and manufacture", page 216, a solid dispersion of gentamicin sulphate and dexamethasone phosphate which is intended to prolong the release. Accordingly, no discussion takes place of the formation of precipitates in the Bayens, et al. reference.

With regard to Renard, et al., (J. Fr. Ophthalmology, 1996, Vol 19, No. 11, pages 689-695), Applicants point out that, as with the reference above, the Renard reference does not teach Applicants' claimed salt comprising a cationic component and an anionic component, but describes eye drops which are described which contain the following combinations:

a) 0.1 % indomethaoin/300 00 IU/10 ml of gentamicin sulphate

b) 0.1 % dexamethasone/350 000 IU/100 ml of neomycln sulphate

Applicants further point out that Indomethacin is a weak carboxylic acid. In Renard, et al., only indomethacin and no salt of indomethacin, such as the sodium salt or potassium salt is mentioned. Being a weak carboxylic acid, indomethacin cannot displace the much more strongly acidic sulphuric acid from its gentamicin salt. For this reason, it is not possible for a gentamicin-indomethacin salt to be formed from indomethacin and gentarnicin sulphate under the conditions indicated in Renard, et al. For this reason, the combination of indomethacin sodium salt present in the solid aggregate state and gentamicin sulphate was used also in Example 5 on page 7 of instant Applicants' specification. A gentamicin.-indomethacin salt can be formed only from soluble salts of gentamicin and indomethacin by reciprocal salt exchange or directly from the free gentamicin base and indomethacin.

In Renard, et al., the combination of dexamethasone and gentamicin sulphate is, moreover, described. In this connection, no low solubility salt can have formed because dexamethasone does not represent an ionic compound and is incapable of salt formation for this reason. Only ionic derivatives such as dexamethasone phosphate are capable of forming low solubility salts (precipitates) with gentamicin sulphate. Accordingly, it is Applicants' position that Applicants' claims are not anticipated by Renard, et al.

Likewise, Applicants point out that Golub, et al., U.S. Patent No. 5,459,135, does not teach Applicants' claimed salt comprising a cationic component and an anionic component. In Golub, there is no disclosure of any salt formation (cation/anion) between the two active agents,

which is an essential feature of Applicants preparations. In Golub, the drugs were simply administered orally with the rats' diet. Nothing points to forming salts of both drugs. Consequently, the references cited by the Examiner do not teach each and every element of the presently claimed invention, and, thus, there is no anticipation.

Respectfully, the burden was on the Examiner to make out a *prima facie* case of anticipation, which required that the Examiner explain where each and every limitation of the instant claims was found in each cited reference. Although the instant claims clearly are drawn to salts, the Examiner's statement of the rejection makes no mention of salts at all.

On the issue of obviousness, the Examiner says if there are any differences, they would appear to be minor and obvious. This is without ever mentioning any particular differences, and without acknowledging that any difference, no matter how seemingly minor, must be dealt with and demonstrated by the appropriate citation of evidence to have been *prima facie* obvious as a matter of law.

In view of the foregoing, Applicants submit that the Examiner would be fully justified to reconsider and to withdraw all rejections. An early notice that the rejections have been reconsidered and withdrawn is, therefore, earnestly solicited.

Applicants believe that the foregoing constitutes a bona fide response to all outstanding objections and rejections.

Applicants also believe that this application is in condition for immediate allowance. However, should any issue(s) of a minor nature remain, the Examiner is respectfully requested to

telephone the undersigned at telephone number (212) 808-0700 so that the issue(s) might be promptly resolved.

Early and favorable action is earnestly solicited.

Respectfully submitted,
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